

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of claims:**

1. (Currently Amended) A method of ~~specifically and selectively~~ up-regulating the gene expression of bone morphogenetic protein(s) in targeted tissue, comprising the steps of:

a. generating at least one specific and selective signal having a frequency from 30 kHz to 120 kHz that when applied to a field generating device operatively disposed with respect to said targeted tissue causes the generation of a field having an amplitude of about 2 to 40 mV/cm in the targeted tissue that is specific and selective for the up-regulation of that ~~has signal characteristics that are selected to up-regulate~~ the gene expression of bone morphogenetic protein(s) (BMPs) in said targeted tissue as measured by mRNA when said ~~field signal~~ is applied to the targeted tissue containing said BMPs; and

b. exposing the ~~bone~~ targeted tissue to ~~a field generated by~~ the specific and selective field generated by said field generating device upon application of said at least one specific and selective signal thereto for a predetermined duration of time at a predetermined intervals duty cycle from approximately 10%-100% so as to selectively up-regulate the gene expression of BMPs in said targeted tissue as measured by mRNA.

2. (Currently Amended) The method of claim 1 wherein the generating step comprises the step of selectively varying the amplitude, duration, duty cycle, frequency, and waveform of the specific and selective signal until ~~the up-regulation of~~ the gene expression of BMPs in said targeted tissue as a result of exposure to the resultant specific and selective field as measured by mRNA in ~~bone~~ the targeted tissue by ~~the generated field~~ is substantially increased.

3. (Currently Amended) The method of claim 1 wherein said generating step comprises the step of generating the specific and selective signal at a remote source and said exposing step comprises the step of applying the field generated by the field generating

device upon application of said specific and selective signal thereto ~~specific and selective signal~~ to the ~~bone~~ targeted tissue.

4. (Currently Amended) The method of claim 3 wherein the exposing step comprises the step of applying the specific and selective signal to at least one electrode electrodes, at least one coil, coil(s) or a solenoid located near the ~~bone~~ targeted tissue.

5. (Currently Amended) The method of claim 4 wherein the exposing step comprises the step of applying the field generated by the field generating device upon application of said specific and selective signal thereto to the ~~bone~~ targeted tissue through one of capacitive coupling and inductive coupling.

6. (Currently Amended) The method of claim 5 wherein when the specific and selective signal is applied to said at least one electrode, said at least one electrode generates causes the electrodes to generate one of a capacitive coupling electric field, and when the specific and selective signal is applied to and the at least one coil coil(s) or solenoid, said at least one coil or solenoid generates to generate an electromagnetic field or a combined field.

7. (Currently Amended) A method for treating at least one of a bone fracture, fracture at risk, delayed union, nonunion, bone defect, spine fusion, osteonecrosis, and osteoporosis, comprising the steps of:

a. generating at least one specific and selective signal having a frequency of 30 kHz to 120 kHz that when applied to a field generating device operatively disposed with respect to targeted tissue causes the generation of a field having an amplitude of about 2 to 40 mV/cm in the targeted tissue that is specific and selective for the up-regulation of that up-regulates the gene expression of bone morphogenetic protein(s) in said targeted tissue as measured by mRNA when said field is applied to the targeted tissue containing said BMPs; and

b. exposing ~~bone~~ the targeted tissue to a ~~field generated by~~ the specific and selective field generated by said field generating device upon application of said at least one specific and selective signal thereto for a predetermined duration of time at a predetermined

~~intervals~~ duty cycle from approximately 10%-100% so as to selectively up-regulate the gene expression of bone morphogenetic protein in said targeted tissue as measured by mRNA.

8. (Currently Amended) The method of claim 7 wherein the exposing step comprises the step of capacitively coupling or inductively coupling the specific and selective field to ~~bone~~ the targeted tissue.

9. (Currently Amended) The method of claim 7 wherein the exposing step comprises the step of applying one of an electromagnetic field and a combined field to ~~bone~~ the targeted tissue.

10. (Currently Amended) The method of claim 7 wherein the generating step comprises the step of generating an electric ~~field~~ signal having ~~an amplitude of approximately 20 mV/cm~~, a sine wave configuration, a duty cycle of approximately 50%, and a frequency of approximately 60 kHz, where the resultant specific and selective field has an amplitude of approximately 20mV/cm in the targeted tissue.

11. (Currently Amended) The method of claim 10 wherein the exposing step comprises the step of applying the ~~electric~~ specific and selective field to the ~~bone~~ targeted tissue for a duration of approximately 24 hours every 24 hours.

12. (Currently Amended) The method of claim 11 wherein the exposing step comprises the step of applying the ~~electric~~ specific and selective field to the ~~bone~~ targeted tissue for a 50% duty cycle of 1 minute ON and 1 minute OFF.

13. (Currently Amended) The method of claim 7 wherein the generating step comprises the steps of selectively varying the amplitude, duration, duty cycle, frequency, and waveform of the specific and selective signal until the up-regulation of the gene expression of bone morphogenetic protein(s) as measured by mRNA in the ~~bone~~ targeted tissue by the resultant generated field is substantially increased.

14. (Canceled)

15. (Canceled)

16. (Currently Amended) A device for the treatment of at least one of bone fractures, fractures at risk, delayed unions, nonunions, bone defects, spine fusion, osteonecrosis, and osteoporosis, comprising a signal source that ~~provides~~ generates at least one specific and selective signal having a frequency of 30 kHz to 120 kHz and a field generating device connected to the signal source so as to receive said at least one specific and selective signal and that is operatively disposed with respect to targeted tissue, said field generating device upon receipt of said at least one specific and selective signal causing the generation of a field having an amplitude of about 2 to 40 mV/cm in the targeted tissue that is ~~that creates a field~~ specific and selective for the up-regulation of the ~~up-regulating~~ gene expression of bone morphogenetic protein(s) in the targeted tissue as measured by mRNA, said signal source controlling and varying duration of time of application of said at least one specific and selective signal ~~and electrodes or coil(s) connected to the signal source that receive said at least one specific and selective signal for application of the field to the bone tissue for a predetermined duration of time at a predetermined intervals~~ duty cycle from approximately 10%-100% so as to selectively up-regulate the gene expression of bone morphogenetic protein(s) in said targeted tissue as measured by mRNA in said ~~bone~~ targeted tissue.

17. (Original) The device of claim 16 further comprising a portable power unit that drives said signal source.

18. (Currently Amended) The device of claim 16 further comprising means for attaching the ~~electrodes~~ field generating device to the body of a patient in the vicinity of bone tissue.

19. (Original) The device of claim 16 further comprising means for attaching the signal source to the body of a patient.

20. (Currently Amended) The device of claim 16 wherein the field generated by application of said at least one specific and selective signal to the field generating device is applied to said ~~bone~~ targeted tissue via one of capacitive coupling and inductive coupling.

21. (Currently Amended) The device of claim 20 wherein the specific and selective signal has a sine wave configuration, a duty cycle of approximately 50%, and a frequency of approximately 60 kHz, where the resultant specific and selective field ~~has and generates an electric field having~~ an amplitude of about 20 mV/cm in the targeted tissue ~~at 60 kHz with approximately a 50% duty cycle~~.

22. (Original) A method of treating at least one of bone fractures, fractures at risk, delayed unions, nonunions, bone defects, spine fusion, osteonecrosis, and osteoporosis comprising the steps of exposing bone tissue to the specific and selective field generated by the device of claim 21 so as to up-regulate gene expression of bone morphogenetic protein(s) as measured by mRNA in the bone tissue.

23. (Original) The method of claim 22, wherein the exposing step comprises the step of applying the specific and selective field to the bone tissue for a duration of approximately 24 hours every 24 hours with a 50% duty cycle of 1 minute on and 1 minute off.

24. (Currently Amended) A method of determining a specific and selective signal that when applied to a field generating device cause the field generating device to generate ~~generates~~ an electric field in targeted tissue that up-regulates bone morphogenetic protein(s) in the targeted tissue, comprising the steps of selecting a starting signal with a signal shape and frequency that when applied to said field generating device causes said field generating device to generate a field that is known to increase or suspected to affect cellular production of bone morphogenetic protein(s), selectively varying a duration of application of said starting signal until a duration that provides a most significant increase in production of BMP(s) is found, selectively varying an amplitude of said starting signal until an amplitude



that provides a most significant increase in production of BMP(s) is found, selectively varying a duty cycle of the starting signal until a duty cycle that provides a most significant increase in production of BMP(s) is found, and selectively varying the duration of an on-off interval of the duty cycle of the signal until an on-off interval that provides a most significant increase in production of BMP(s) is found.

25. (Currently Amended) A method as in claim 24, comprising the further steps of selectively varying a frequency and waveform of said starting signal, keeping other signal characteristics constant, until a greatest increase in the gene expression of BMP as measured by mRNA is found.

26. (New) The device of claim 16, wherein the field generating device comprises at least one electrode, at least one coil, or a solenoid.